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Utility of Administrative Databases and Big Data on Understanding Glioma Treatment—A Systematic Review

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Abstract

Background Gliomas are a heterogeneous group of tumors where large multicenter clinical and genetic studies have become increasingly popular in their understanding. We reviewed and analyzed the findings from large databases in gliomas, seeking to understand clinically relevant information.

Methods A systematic review was performed for gliomas studied using large administrative databases up to January 2020 (e.g., National Inpatient Sample [NIS], National Surgical Quality Improvement Program [NSQIP], and Surveillance, Epidemiology, and End Results Program [SEER], National Cancer Database [NCDB], and others).

Results Out of 390 screened studies, 122 were analyzed. Studies included a wide range of gliomas including low- and high-grade gliomas. The SEER database ($n = 83$) was the most used database followed by NCDB ($n = 28$). The most common pathologies included glioblastoma multiforme (GBM) ($n = 67$), with the next category including mixes of grades II to IV glioma ($n = 31$). Common study themes involved evaluation of descriptive epidemiological trends, prognostic factors, comparison of different pathologies, and evaluation of outcome trends over time. Persistent health care disparities in patient outcomes were frequently seen depending on race, marital status, insurance status, hospital volume, and location, which did not change over time. Most studies showed improvement in survival because of advances in surgical and adjuvant treatments.

Conclusions This study helps summarize the use of clinical administrative databases in gliomas research, informing on socioeconomic issues, surgical outcomes, and adjuvant treatments over time on a national level. Large databases allow for some study questions that would not be possible with single institution data; however, limitations remain in data curation, analysis, and reporting methods.

Keywords
- administrative database
- glioma
- glioblastoma

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Introduction

Gliomas encompass the second most common type of brain tumor in the United States, while glioblastoma multiforme (GBM) accounts for the most common malignant primary brain tumor.[1] Multiple advances in treatment, including earlier imaging and detection, safer surgical resection, and adjuvant radiochemotherapy (RCT) have improved disease treatment.[2] Clinical variables, such as age and surgical resection, in addition to genetic factors have been helpful in stratifying patient risk. However, there remains heterogeneity in the outcomes of patients and treatment response.

The rise in the use of administrative databases and big data has been notable in neurosurgery, but their impact on glioma understanding remains limited.[3] These studies often show multiple associative findings due to their significant sample sizes without distinction between statistical and clinical significance. Moreover, the clinical impact of these studies remains unclear. The purpose of this review was to accumulate and compare the lessons learned from big data regarding gliomas and identify future challenges for exploration.

Methods

We aimed to evaluate the impact of multicenter, publicly available administrative databases on clinically relevant information in the treatment of gliomas. A literature search of PubMed was performed using the following search terms: (National Surgical Quality Improvement Program OR NSQIP OR National Inpatient Sample OR NIS OR HCUP-NIS OR Kid's Inpatient Database OR HCUP-KID OR Surveillance, Epidemiology, and End Results Program OR SEER OR Pediatric Health Information Systems OR PHIS OR MarketScan OR Administrative database OR SEER OR SEER-Medicare OR CBTRUS OR NCDB OR NRD OR SID OR SASD OR CMS OR Vizient OR Premier OR PearlDiver OR Optum) AND (glioma OR glioblastoma OR astrocytoma OR oligodendroglioma OR anaplastic astrocytoma OR anaplastic oligodendroglioma [AO]). References from manuscripts were also reviewed to identify relevant studies.

Studies up to January 2020 and English-only manuscripts were included. Studies were reviewed independently by two reviewers (M.O., M.K.) to exclude case reports, reviews, and laboratory studies. The main study findings including prognostic factors, sample number, database type, World Health Organization (WHO) tumor status, tumor types, surgical complications, and surgical outcomes were noted. Papers were narrowed to those discussing low-grade glioma (LGG), including grade II gliomas, astrocytoma and oligodendroglioma, as well as high-grade gliomas (HGG), including anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), and GBM. Studies used a combination of histological and molecular classification, depending on the year of study. Several studies incorporated other glioma types that were excluded (**Supplemental discussion, ►Fig. S1, ►Table S1).** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to draft this manuscript. Descriptive statistics are demonstrated where relevant.

Results

A total of 390 studies were screened and narrowed down to 122 studies (►**Fig. 1**). Studies included AA only ($n = 2$), AA with other pathologies ($n = 3$), AO only ($n = 2$), GBM ($n = 67$), grades II to IV glioma ($n = 31$), grade II glioma ($n = 3$), HGG ($n = 7$), mix of high-grade tumors ($n = 1$), and oligodendroglioma ($n = 6$) (►**Table 1**). The most common databases included the NCDB ($n = 28$) and SEER databases ($n = 83$). A further breakdown of all studies into LGG and HGG was performed (►**Figs. S1–S3**).

Low Grade Glioma

LGGs were evaluated as an aggregate group in three studies. One study on grade II gliomas showed that RCT did not improve survival compared with chemotherapy alone,[4] and two others showed that greater extent of resection (EOR) improved prognosis.[5,6] Unfortunately, these studies were limited by aggregating all LGGs, which often behave distinctly.

Six studies specifically evaluated oligodendroglioma,[7–12] with two of these studies showing improved survival over the preceding 10 years (e.g., 2004–2013) mainly as a function of improved surgery and RCT.[9,12] Achey et al evaluated the age-adjusted incidence rate from the Central Brain Tumor Registry of the United States from 2000 to 2013.[7] A decreased incidence of oligodendroglioma and AO was seen, although this was possibly because of recent changes in molecular classification. Prognostic factors impacting survival for oligodendrogliomas in other studies included age, sex, race, and EOR.[8,10–12] Alattar et al evaluated 3,406 patients with oligodendroglioma from 1999 to 2010 using the SEER database and demonstrated an improvement in OS after gross-total resection compared with AA or GBM.[8] This finding was confirmed by Kinslow et al in their evaluation of 3135 cases from the SEER database data from 2004 to 2013; they also showed that EOR impacted survival in both oligodendroglioma and AO.[10]

Multiple studies have evaluated glioma by including either LGG as a broad category or comparing LGG with HGG.[1,13–37] Several studies evaluated the epidemiology of gliomas and demonstrated increased likelihood in Caucasians, older, or male patients, patients with prior smoking history, women with prior breast cancer treatment, and insured patients.[13–16,19] Plascak et al evaluated 24,230 glioma patients using the SEER database between 2000 and 2006; they showed a greater incidence of gliomas in countries with higher socioeconomic status, which suggested unequal distribution of diagnostic resources.[19] Another study using the SEER database noted a decreasing incidence of gliomas and suggested there was a shift to increased diagnosis of GBM by pathological criteria over time.[18] The vast majority of studies involving glioma have looked at prognostic factors. These studies have suggested that White race, younger age, more

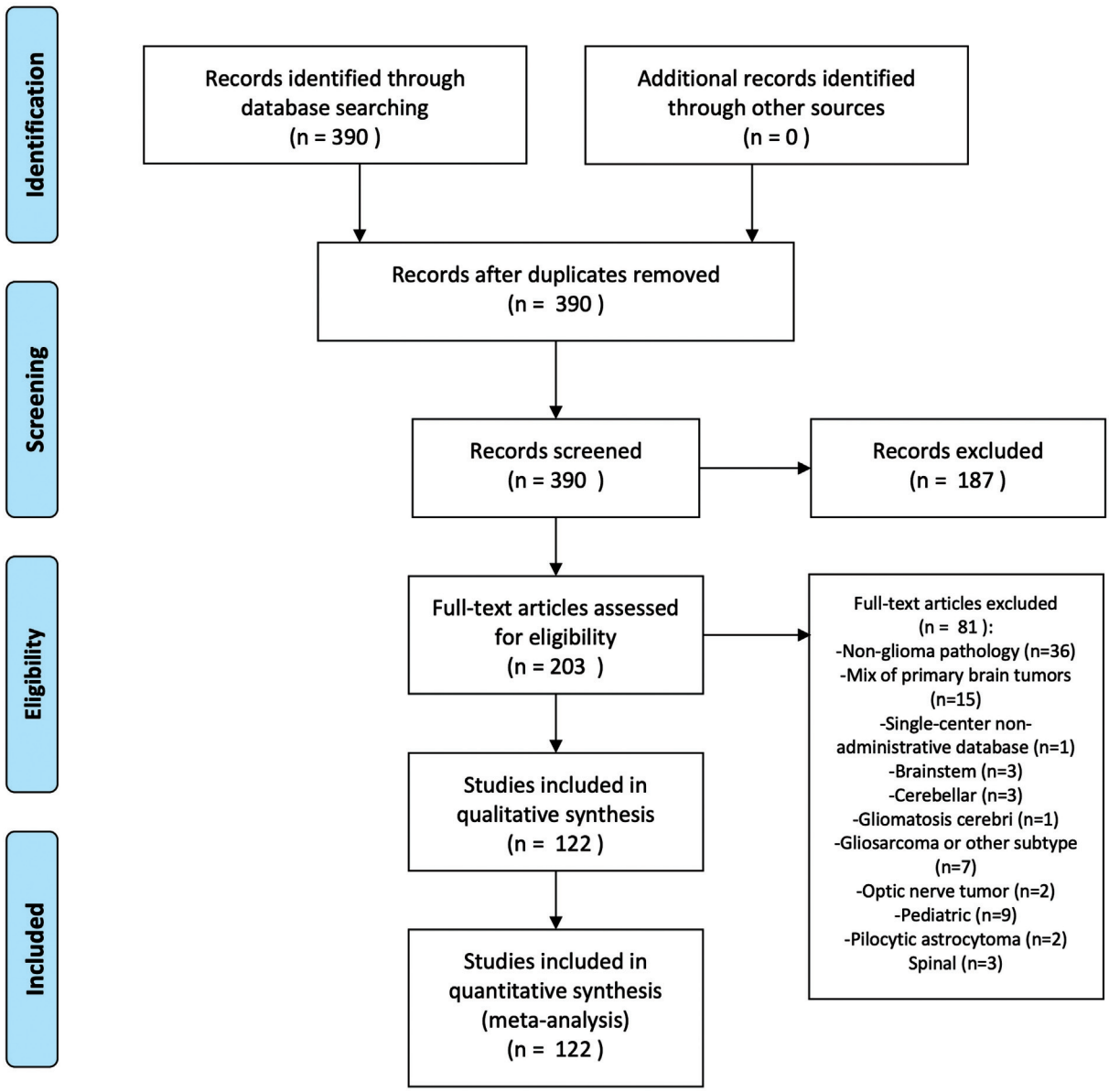

Fig. 1 The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of selected studies.

recent diagnosis, lower WHO grade or histology, marital status, better socioeconomic status, EOR, radiotherapy, radiochemotherapy, treatment at high-volume facilities, and tumor size positively impact patient prognosis.[1,4,16,17,20–36] Missios et al evaluated 21,384 cases of glioma between 2005 and 2011 using the National Inpatient Sample (NIS) database and showed that perioperative complications were increased by greater age, coagulopathy, coronary artery disease, congestive heart failure, and smoking history.[37]

Although these studies have had an impact by identifying consistent risk and prognostic factors, they are limited by aggregating glioma types, mostly as a limitation of lacking molecular data in nearly all multicenter databases. Moreover, both epidemiology and prognostic factor studies suggest geographic differences in outcomes because of medical resources and facilities but do little to address these inequalities or report in sufficient detail to confer actionable insight. Despite improve standardization of glioma treatment with clinical guidelines, treatment variation likely still occurs, which is impacted by patient socioeconomics and remains poorly understood.

High-Grade Glioma

Several studies have evaluated and compared outcomes for AA and AO. Prognostic factors for AA included age, RCT, private insurance, higher income, tumor site, marital status, EOR, histology, and treatment with RT.[38–44] Smoll et al specifically looked at 3,202 patients with AA between 1973 and 2006 in the SEER database, showing worsened mortality compared with matched controls.[43] A 5- and 10-year overall survival (OS) of 23.6% and 15.1% was identified, respectively. Age significantly impacted prognosis, however, improvement in survival was not seen over the study time period. In contrast, Shin et al evaluated 1,692 patients with

Table 1 Studies evaluating administrative studies/big data in LGG and HGG

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
NCDB	AA	4,807	2004–2013	Prognostic factors: RCT, age, private insurance, higher income	Shin[40]
SEER	AA	3,202	1973–2006	5-year OS 23.6%; prognostic factor: age (only 3 years postdiagnosis); 5 year survival unchanged over time	Smoll[43]
SEER	AA, AO	1,939	1973–2013	Prognostic factors: age, tumor site, marital status, EOR, histology, RT, surgery	Zhao[44]
SEER	AA, AO	390	1990–2008	Evaluated patients > 70 years of age; median OS 11 month; prognostic factors: EOR, RT, gender, marital status	Mukherjee[38]
SEER	AA, GBM	24717	1999–2010	Median OS (AA versus GBM with GTR) 64 versus 13 months; prognostic factors: EOR	Padwal[39]
NCDB	AO	1,643	2004–2013	Prognostic factors: race, age, RCT	Shin[42]
NCDB	AO	1,692	2004–2013	5-year OS 59.8%; prognostic factors: RCT, single-agent chemotherapy	Shin[41]
NCDB	GBM	100,672	1998–2011	Median OS 7.5 months; prognostic factor: age, tumor histology, race, gender, education, insurance status, EOR, RCT, tumor location	Dressler[56]
NCDB	GBM	60,672	2004–2013	Median OS 8.1 months; prognostic factors: TMZ, high volume facility treatment; 2-month survival benefit in high-volume centers	Aulakh[55]
NCDB	GBM	738	2010–2012	Median OS (RCT) 15.6 months, 2-year OS 25.9%; limited benefit of RT in patients with MGMT methylation	Lee[60]
NCDB	GBM	448	2010–2013	Median OS (RCT) 8.7 months; prognostic factors: age, EOR, RCT;	Malakhov[59]
NCDB	GBM	4,598	1998–2011	Prognostic factor: long-course radiotherapy compared with short-course radiotherapy	Mak[58]
NCDB	GBM	114,979	1998–2012	Prognostic factor: RCT compared with radiation alone	Glaser[57]
NCDB	GBM	114,979	1998–2012	Prognostic factors: disparities in standard of care secondary to race, insurance status and institution of treatment	Rhome[65]
NCDB	GBM	5,252	2004–2012	Prognostic factor: single-agent chemotherapy with radiotherapy in elderly patients	Huang[111]
NCDB	GBM	89,839	2004–2013	Prognostic factor: patients treated in academic/research programs, high-volume centers	Hauser[64]
NCDB	GBM	27,865	2004–2013	Prognostic factor: GTR; no survival benefit of STR over biopsy	Trifiletti[67]
NCDB	GBM	1,223	2004–2014	Dose escalation not associated with survival; prognostic factors: age, comorbidity score, hospital volume (noncommunity centers), education level, income, insurance status, race, gender	Wegner[68]
NCDB	GBM	45,942	2004–2015	Prognostic factor: younger age, female gender, black ethnicity, higher KPS, and GTR over STR; delay > 8 weeks for radiochemotherapy detrimental after GTR; delay < 4 weeks for radiochemotherapy detrimental after STR	Buszek[62]
NCDB	GBM	45,268	2004–2016	Median OS was 12.8 months vs 8.3 months for patients with unifocal GBM or multifocal	Haque[63]

(*Continued*)

Table 1 (*Continued*)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				GBM; prognostic factor: radiochemotherapy; radiochemotherapy beneficial even if multifocal	
NCDB	GBM	13,489	2005–2012	Prognostic factors: delay in radiochemotherapy treatment	Yusuf[76]
NCDB	GBM	1,479	2006–2011	Prognostic factor: radiochemotherapy compared with radiation alone	Kole[66]
NCDB	GBM	12,725	2010–2012	Median OS (MGMTme versus MGMT-) 20 versus 15 months; prognostic factors: RCT in MGMTme tumors	Lee[61]
NCDB; RTOG	GBM	40,396	1974–2002	Survival for patients in the RTOG database exceeded survival in patients in the NCDB group likely because patients in the RTOG database come from clinical trials which have specific enrollment criteria; prognostic factor: age	Siker[73]
SEER	GBM	9,103	1973–2006	Prognostic factor: age, marital status, resection	Walker[75]
SEER	GBM	21,783	1973–2007	Prognostic factors: EOR, RT	Zinn[77]
SEER	GBM	34,664	1973–2008	Prognostic factor: race (Asian/Pacific Islander), surgical resection, age, RT; improved survival over time	Thumma[74]
SEER	GBM	51,518	1973–2014	Prognostic factor: no prior history of cancer	Al-Husseini[70]
SEER	GBM	60,456	1973–2015	Prognostic factors: age, tumor size, tumor location, GTR, radiation, chemotherapy, brachytherapy	Bartek[72]
SEER	GBM	25,117	1985–2014	Prognostic factors: Hispanic Latino (GBM and GBM-GC), age, gender	Bin Abdulrahman [120]
SEER	GBM	10,987	1988–2001	Prognostic factors: marital status	Chang[78]
SEER	GBM	1,530	1991–1999	Prognostic factor: race	Barnholtz-Sloan [71]
SEER	GBM	1,375	1991–2002	Median time post-resection to initiation of RT was 15 days; no impact of wait time on OS	Lai[121]
SEER	GBM	1,273	1991–2007	No difference in patient outcomes between low- and high-readmission rate hospitals	Nuno[117]
SEER	GBM	19,674	1993–2007	Improved survival over time	Darefsky[80]
SEER	GBM	4,137	1994–2002	Prognostic factors: age, marital status, and comorbidities	Iwamoto[81]
SEER	GBM	1,652	1995–2009	Median OS of 7.4, 5.9 and 5.6 months for TMZ/RT, RT alone (2005–2009) and RT alone (1995–1999), respectively; benefit of TMZ addition to RT in later years	Arvold[98]
SEER	GBM	3,963	1997–2010	GTR supported as initial treatment and for recurrence	Chen[122]
SEER	GBM	3,784	1997–2010	Patients with postop infections showed no significant difference in survival	Chen[123]
SEER	GBM	22,777	1998–2007	Factors associated with omission of RT included older age, lower annual income, African–American race, Hispanic race, Asian–American race, unmarried status, and STR/Bx; use of radiation associated with improved OS	Aizer[69]
SEER	GBM	10,022	1998–2008	Patients surviving past 2 years have favorable conditional probability of survival	Johnson[83]
SEER	GBM	20,705	1998–2009		Noorbakhsh[86]

Table 1 (*Continued*)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				Benefit of 2–3 months survival after GTR in all age groups; lower rate of GTR in older patients	
SEER	GBM	342	1998–2009	Median OS 12 months; prognostic factors: EOR	Adams[82]
SEER	GBM	6,039	1999–2010	Prognostic factors: gender (female), married patients, ethnicity	Shah[89]
SEER	GBM	13,932	2000–2008	Benefit of TMZ to survival over time	Johnson[84]
SEER	GBM	6,586	2000–2008	Prognostic factor: gender (female)	Tian[90]
SEER	GBM	20,879	2000–2009	Benefit of TMZ and BZM to survival over time	Wachtel[91]
SEER	GBM	302	2000–2010	Prognostic factors: supratentorial location, GTR, and later year of diagnosis	Lam[85]
SEER	GBM	14,675	2000–2010	Median OS 11 months; prognostic factors: age, gender, marriage status, race (non-Hispanics), region (northeast), nonlateralizing, small (< 3 cm), adjuvant radiation	Pan[87]
SEER	GBM	26,481	2000–2010	Prognostic factors: age, gender, race (non-White), socioeconomic status	Porter[88]
SEER	GBM	28,933	2000–2013	Improved survival with TMZ with radiation and adjuvant TMZ and then BEV after FDA approval	Zhu[92]
SEER	GBM	20,550	2000–2013	Prognostic factors: tumor size (< 5 cm), EOR, RCT	Shu[96]
SEER	GBM	6,919	2001–2006	Benefit of TMZ to survival over time	Koshy[94]
SEER	GBM	11,189	2001–2006	Cure fraction of 12% for young adults at 10 years	Smoll[97]
SEER	GBM	21,184	2001–2011	Prognostic factors: race (Latinos); possibly greater incidence of GBM-GC in Latinos	Shabihkhani[95]
SEER	GBM	5,991	2004–2008	Prognostic factors: age, marital status, median income; factors led to increased GTR and RT	Aneja[93]
SEER	GBM	24,262	2004–2013	Regional differences in survival and incidence in the US; prognostic factors: age, marital status, race, tumor laterality, WHO grade, disease extent, tumor size, tumor extension, RCT	Xu[119]
SEER	GBM	24,348	2004–2013	Median survival 15, 15 and 5 months for pediatric, adult, and elderly, respectively	Li[116]
SEER	GBM	30,767	2004–2015	Prognostic factors: marriage, age, race, middle-income counties	Xie[52]
SEER	GBM	5,607	2006–2010	Median OS of 8, 7, and 9 months in 2006, 2008, and 2010, respectively; improved survival with BZM	Johnson[105]
SEER	GBM	2,603	2006–2011	Benefit of BZM to survival	Davies[102]
SEER	GBM	13,665	2007–2012	Prognostic factors: insurance status, RT, marital status; improved OS over time	Rong[110]
SEER	GBM	3,473	2010–2014	Prognostic factors: race (Asian–Pacific Islander)	Bohn[101]
SEER; Broad Institute Genotype Tissue Expression project; UCSF 10K Immunomes-database	GBM		1973–2016	Increased expression of immunoregulatory molecules in the elderly	Ladomersky[106]
	GBM	5,029	1999–2007	Median survival was 4.9 months	Arvold[99]

(*Continued*)

Table 1 (*Continued*)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
SEER; Medicare database					
ACS-NSQIP	GBM	1,016	2012–2016	Patients' aged 65–89 years included; 3.4% 30-day death rate; 5.7% severe complication rate; 33% change in living disposition rate	Rahmani[109]
California Office of Statewide Health Planning & Development inpatient-discharge administrative database	GBM	18,506	1995–2010	13.2% 30-day readmission rate; each readmission represented an additional $20,296 in median hospital charges on top of the $72,029 in charges for the index neurosurgical admission	Marcus[107]
MarketScan	GBM	14,037	2007–2016	Functional mapping associated with decreased complications, reoperations, emergency department visits, and shorter lengths of stay; no difference in charges with functional versus no mapping	Pendharkar[108]
SEER	GBM	48748	2000–2013	Multiple primary tumors associated with female gender, White race, smaller tumors	Nguyen[112]
SEER	GBM	12,437	2002–2011	Hospice enrollment associated with older age, female gender, higher education, White race, lower median income	Forst[104]
Los Angeles County Cancer Surveillance Program, CCR, and SEER	GBM	38,567	1996–2006	Increased incidence of frontal, temporal and cerebellar GBM over time compared with other locations	Zada[113]
SEER	GBM	21,493	1973–1997	Prognostic factor: race (white)	Barnholtz-Sloan [100]
SEER	GBM	1,181	1973–2015	Prognostic factors (for secondary malignancy): age, race, differentiated grade of cancer tissue, marital status, WHO grade, latency	Wang[118]
SEER	GBM	37,581	2001–2011	Median OS 14 versus 11 months of metropolitan versus non-metropolitan; prognostic factors: urban area	Delavar[103]
FCDS	Glioma	14,092	1981–2013	Diagnostic factor: race (Caucasian more likely), age (older), gender (male), smoking status, insurance status	Persaud-Sharma [15]
NCDB	Glioma	49,405	2004–2013	Proton beam therapy better median and 5-year OS compared with other radiation therapy	Jhaveri[17]
NCDB	Glioma	5,036	2010–2014	Prognostic factors: female gender (GBMs)	Gittleman[20]
NIS	Glioma	21,384	2005–2011	Identified perioperative complication risk: age, coagulopathy, CAD, CHF, smoking	Missios[37]
SEER	Glioma	5,956	1973–2010	Prognostic factor: race (White)	Samaan[21]
SEER	Glioma	49,124	1973–2014	Increased incidence of GBM versus non-GBM over time	Li[18]
SEER	Glioma	389,415	1973–2014	Increased risk of gliomas in younger women after breast cancer treatment	Mezencev[14]
SEER	Glioma	58,700	1975–2016	Prognostic factor: age	Zhou[124]
SEER	Glioma	22,427	1977–2000	Prognostic factors: age, gender, year of diagnosis; diagnostic factors: age, gender, later year of diagnosis	Hess[16]
SEER	Glioma	24,340	1992–2007	Diagnostic factors: age, race (non-Hispanic White)	Dubrow[13]
SEER	Glioma	1,067	1994–2002	Median OS 9, 4, 57 and 9 months for low-grade glioma, AA, OG, and AO, respectively; prognostic factors: age, WHO grade	Iwamoto[25]
SEER	Glioma	9,385	1999–2010		Dong[24]

Table 1 (*Continued*)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				Improved survival for grade II and III gliomas over time	
SEER	Glioma	24,230	2000–2006	Greater incidence gliomas in counties with higher socioeconomic status	Plascak[19]
SEER	Glioma	617	2000–2014	Prognostic factor: marital status	Long[26]
SEER	Glioma	244,808	2000–2014	Prognostic factor: race; non-Hispanic whites showed lower survival	Ostrom[1]
SEER	Glioma	43,324	2000–2016	Prognostic factor: marital status	Xie[28]
SEER	Glioma	50,170	2003–2012	Prognostic factor: socioeconomic status	Deb[23]
SEER	Glioma	10,591	2005–2013	Prognostic factor: age, race (White), non-cerebral tumor sites	Sun[51]
SEER; Medicare database	Glioma	1,958	1991–1999	Prognostic factors: age, EOR, RT	Barnholtz-Sloan [50]
NCDB	Glioma	1,029	2004–2012	No difference between single- and multi-agent chemotherapy	Haque[125]
NCDB	Glioma	2,253	2004–2013	Prognostic factor: RCT	Wu[27]
NCDB	Glioma	5,539	2004–2014	Prognostic factor: high-volume facility	Zhu[29]
NCDB	Glioma	1,952	2010–2012	Prognostic factor: histology, RT	Youseff[36]
NCDB	Glioma	1,032	2010–2013	Prognostic factor: WHO grade, tumor size	Jairam[32]
SEER	Glioma	2,009	1973–2001	Prognostic factor: gender (female), age, race (White), WHO grade, later year of diagnosis; improved survival over time	Claus[30]
SEER	Glioma	2,825	1973–2011	Indicated lack of OS improvement for LGG; suggested importance of molecular markers	Claus[31]
SEER	Glioma	42,622	2000–2013	Evaluated primary and secondary GBM	Nguyen[34]
SEER	Glioma	5,037	2001–2006	Patients diagnosed with LGG 17X more likely to die than general population; older patients with LGG 31X more likely to die than young adults in first year	Smoll[35]
SEER	Glioma	3,732	2004–2013	Prognostic factors: age, marital status, tumor site, histological type, tumor size, surgery, and sex	Zhao[22]
SEER	Glioma	561	2006–2012	Prognostic factor: EOR	Diaz-Aguilar[126]
SEER, TCGA	Glioma	1,278	1999–2016	Overlap of risk genes in Alzheimer disease and gliomas (TREM2, SPI1, CD33, and INPP5D)	Lehrer[33]
NCDB	Grade II glioma	1,054	2004–2013	RCT not associated with higher survival in comparison to chemotherapy alone	Jhaveri[17]
SEER	Grade II glioma	1,980	1999–2010	Prognostic factors: frontal lobe location, EOR, age	Alattar[5]
SEER	Grade II glioma	4,113	1999–2010	Prognostic factors: EOR	Schupper[6]
CSP	HGG	2,743	1990–2000	5-year OS 6%; median OS 6.6 months; improved survival over time; prognostic factors: age, WHO grade, tumor site, primary treatment, year of treatment, academic hospital	Tsao-Wei[45]
PMSI	HGG	1,659	2010–2018	Median OS was 1.4 years; prognostic factors: carmustine wafer, age, gender, recurrent disease	Champeaux[46]
MarketScan and Medicare supplemental health claims database	HGG	2,157	2009–2015	No significant association between use of BEV and occurrence of thromboembolic events	Lee[53]

(*Continued*)

Table 1 (*Continued*)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
SEER	HGG	154	1973–2013	Median OS 10 months; prognostic factors: non-brainstem location, RT	Maxwell[47]
SEER	HGG	353	1973–2015	Prognostic factors: age; no tumor-related characteristics were associated with survival	Yang[49]
SEER	HGG	14,461	1998–2007	Prognostic factor: WHO grade, RT	Rusthoven[48]
SEER	HGG	3,706	2000–2013	Median OS 14.3 month; 5-year OS 6.2%; prognostic factor: age, location (unilateral), EOR, RT	Xia[127]
ACS-NSQIP	Mix of malignant brain tumor	4,407	2007–2012	Perioperative steroid use associated with shorter hospitalization and increased readmission; no adverse events with steroid use	Alan[54]
CBTRUS	Oligodendroglioma		2000–2013	OD and AOD showed decreased incidence over time	Achey[7]
SEER	Oligodendroglioma	762	1973–2012	Prognostic factors: age, gender, race; improved survival over time	Furst[12]
SEER	Oligodendroglioma	7,001	1973–2013	Prognostic factor age	Lau[11]
SEER	Oligodendroglioma	3,406	1999–2010	Prognostic factors: EOR; limited benefit for GTR in OG compared to AA or GBM	Alattar[8]
SEER	Oligodendroglioma	3,880	1999–2012	Improved survival over time	Brandel[9]
SEER	Oligodendroglioma	3,135	2004–2013	Prognostic factors: EOR	Kinslow[10]

Abbreviations: AA anaplastic astrocytoma; AO, anaplastic oligodendroglioma; ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program database; BZM, bevacizumab; CA, California; CBTRUS, Central Brain Tumor Registry of the United States; CAD, coronary artery disease; CCR, California Cancer Registry; CHF, congestive heart failure; CSP, Cancer Surveillance Program; EOR, extent-of-resection; FCDS, Florida Cancer Data Registry; GBM, glioblastoma multiforme; GTR, gross total resection; HGG, high-grade glioma; LGG, low-grade glioma; NCDB, National Cancer Database; NIS, National Inpatient Sample; OS, overall survival; PMSI, French medico-administrative national database; RT, radiotherapy; RTOG, Radiation Therapy Oncology Group; SEE, Southern and Eastern Europe Tumor Registry; SEER, Surveillance, Epidemiology and End Results Database; TCGA, The Cancer Genome Atlas; TMZ, temozolomide; UCSF, University of California - San Francisco.

AO via the NCDB database between 2004 and 2013.[41] An overall 5-year of 59.8% was seen and significant benefits in survival were seen from RCT or single-agent chemotherapy. Patients were more likely to receive adjuvant RCT if treated in later time epochs, were male, had private insurance, or had $\geq$ \$63,000 median income. While the survival benefit from AOs compared with AAs were not unexpected, differences in treatment with RCT often depended on socioeconomic factors.

HGG also represent a diverse group of studied pathologies commonly aggregated in database studies. Tsao-Wei et al showed improved survival in HGG in Los Angeles County over time between 1990 and 2000.[45] In addition, this study showed relative improvement in survival of GBM compared with grade III gliomas over the same time period despite an OS of 6% at 5-years for the study group. Several other studies regarding HGG have studied several prognostic factors including age, gender, recurrent disease, tumor location, WHO grade, primary treatment, RT, and EOR.[28,45–52] Another study by Lee et al showed no association between bevacizumab use and thromboembolic events.[53] One study evaluated 4,407 patients via the NSQIP database who underwent resection of a malignant brain tumor between 2007 and 2012. This study included metastatic tumors ($n = 1611$) and malignant gliomas ($n = 2796$).[54] Steroid use was found to decrease hospital length of stay but increase risk of readmission in an unmatched case-control analysis; however, these findings were not confirmed on a propensity matched analysis.

Glioblastoma

Studies on GBM encompass the largest topic of database analysis in gliomas. A total of 68 studies were published between 2002 and 2020 (►**Table 1**). Studies evaluating prognostic factors showed that age, tumor histology, molecular markers, race, sex, education, marital status, treatment in high-volume and/or urban centers, insurance status, EOR, RCT, and tumor location impacted outcomes.[52,55–111] Although a few studies simply described general demographic changes of GBMs,[112,113] most studied specific questions.[52,55–91,93–110,114–116] Most studies also demonstrated improved survival over time, which was likely associated with an increased use of RCT, temozolomide, and adjuvant treatments, such as bevacizumab, but could not deliver more granular specifics.

The impact of facility type and location on outcome after GBM treatment has been evaluated by several studies. Aulakh et al[55] evaluated 60,672 patients in the NCDB from 2004 to 2013, demonstrating that treatment in a high-volume facility, along with temozolomide treatment,

improved survival. In fact, treatment in a high-volume center conferred a 2-month OS benefit. Another study by Hauser et al[64] evaluating 89,839 patients in the NCDB from 2004 to 2013 suggested better outcomes for patients treated in academic centers, and a study by Delavar et al.[103] evaluating 37,581 patients between 2001 and 2011 showed a 3-month improvement in OS for patients living in metropolitan areas compared with nonmetropolitan areas. Other studies support the impact of institution type on treatment accessibility and outcome.[65,68] Nuno et al[117] evaluated 1,273 patients in the SEER database between 1991 and 2007 to compare hospitals with low and high rates of readmission after GBM treatment. No differences were seen in patient outcomes such as complications, nonroutine discharge, length of stay, EOR, or OS. Thus, facility characteristics, such as patient volume and facility location, seemed to impact outcome.

Several studies have evaluated the impact on outcome of socioeconomic factors, namely, marital status, race/ethnicity, and insurance status. Several studies have shown the positive impact of marriage on outcome after GBM.[52,56,68,69,75,78,87,89,104,110,118] Several studies have shown the impact of race on outcome, primarily demonstrating that non-White races fared worse.[52,69,71,74,87,89,95,100,101,104,118,119] Aizer et al[69] studied 22,777 patients between 1998 and 2007 via the SEER database and showed that factors associated with omission of RT included African-American and Asian-American races, unmarried status, and lower annual income. Other factors associated with reduced likelihood of RT included older age and subtotal resection/biopsy. Forst et al[104] evaluated 12,437 patients via the SEER database between 2002 and 2011, showing that hospice enrollment was associated with higher education, White race, and lower median income among other factors. Studying 13,665 patients in the SEER database between 2007 and 2012, Rong et al[110] showed that insurance status highly affected prognosis. Patients who were uninsured or had Medicaid coverage were likely to be younger and unmarried and to present with larger tumors. In addition, incremental survival benefits from 2007 through 2011 were seen in insured patients but not uninsured patients.

Discussion

An evaluation of the use of administrative databases and big data in the study of gliomas demonstrated 122 studies across a wide range of pathologies and clinical questions. While we aimed to characterize the important prognostic factors seen across various geographic locales and significant time frames, there remained limitations in the granular study details important to clinical applicability. Several factors, including age, tumor grade and histology, as well as surgical EOR and adjuvant therapies, were reliably impactful on patient survival which were unsurprising. More specific patient situations or treatments that offer insight to treatment could often not be determined based on the database structure. Other prognostic factors often were not reproducible among different studies. Numerous studies show improvement in survival rates over time and loosely attribute this to improved surgical technique and optimal timing of adjuvant RCT. But the impact of specific treatment changes could not be identified from these databases. The incorporation of molecular diagnostics in the discussion of these patients was commonly lacking and multiple studies combined different pathologies or WHO grade tumors to report findings.

One of the major advantages of large databases is the ability to compare across variation of socioeconomic factors, such as race, marital status, and insurance status, which would not be possible for many individual centers which have more homogeneous patient populations. This allows tracking of outcomes in disadvantaged patients and raises awareness for the patient management. In addition, some studies have shown the improvement of survival for patients in high-volume centers or metropolitan areas, suggesting variation in care delivery. However, the major disadvantage of large databases involves higher level of detail regarding patients and tumor types. These group of studies also did not indicate avenues to improve on health care disparities despite detecting them multiple times.

Improved analysis of large administrative databases is still needed. Despite some reported benefits, large databases are generally not designed to address all clinically relevant study questions with precision. One example of this is that different studies can show contradictory results for various prognostic factors. This may be likely a result of patient heterogeneity or the statistical analysis performed. Use of traditional statistical methods have the potential to identify statistically significant but not clinically relevant findings. Improvements are needed in our ability to analyze data from large administrative databases to ensure we can answer impactful questions and recognize reproducible epidemiologic patterns. Use of uniform reporting criteria for these studies, such as the STROBE criteria, is also necessary to improve the quality of these studies.

Conclusions

This study helped identify databases involved in the understanding of treatment for various gliomas. Descriptive information regarding the involved databases is provided. Consistent prognostic factors included age, tumor grade, histology, and EOR. While improvement in survival was seen over time, it was unclear which treatments specifically impacted this. In addition, marked socioeconomic, and racial disparities in health care persisted over time for a variety of pathologies. Administrative databases were also limited in integrating updates in molecular tumor subtypes. The application of insights from research databases to impact patient care remains inadequate.

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Conflict of Interest
None declared.

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